NATIONAL
SCIENCE
ADVISORY
BOARD FOR
BIOSECURITY

Responsible Communication of Life Sciences Research with Dual Use Potential

A Set of Communication Tools
Excerpted from the NSABB's Proposed Framework for the Oversight of Dual Use Life Sciences Research[1]

Contents

[1] NSABB, *Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information* (National Institutes of Health, June 2007), http://oba.od.nih.gov/biosecurity/pdf/Framework%20for%20transmittal%200807_Sept07.pdf.

1. Introduction

One of the major charges to the NSABB is to recommend strategies to help ensure that research information with dual use potential is communicated responsibly, in a manner that addresses both biosecurity concerns and the need for open sharing of research results and technologies so that the research can be validated and used for further research. Toward this end, the NSABB developed a set of tools to facilitate consistent decisionmaking about the responsible communication of research information with dual use potential.

These tools consist of:

- A set of principles for the responsible communication of research with dual use potential
- Points to consider for identifying and assessing the risks and benefits of communicating research information with dual use potential, including options for the communication of such research information
- Considerations for the development of a communication plan for research with dual use potential

It is important to note that it is *not* the intent of the NSABB that every potential communication of research—be it an abstract, poster, seminar, or manuscript—be assessed using the communication tools. Rather, the tools may be utilized for the subset of life sciences research or research information determined to be dual use research of concern.

Because research findings are communicated at many points along the research continuum (e.g., during project concept and design, in funding applications, in seminars, and in publication of manuscripts), it is important to be aware of the potential for misuse of information at every point. The communication tools are designed to help individuals identify and assess the risks and benefits of communicating information with dual use potential. The tools can be employed by a variety of users in a number of settings. These include researchers who are developing research proposals; investigators engaged in dual use research who are preparing abstracts, posters, seminars, and manuscripts about their work; and individuals involved in the prepublication review of such information, such as research supervisors and administrators, peers, and dual use research review entities. The tools might also be useful to the scientific publishing community and for science ethics courses.

The variety of potential uses and users of these communication tools makes it likely that not all aspects of the tools will be applicable at all times. Thus, users are encouraged to tailor and format the tools for their specific purpose(s). For example, students in an ethics course might use the "Points To Consider in Assessing the Risks and Benefits of Communicating Research Information With Dual Use Potential" to analyze actual manuscripts, and so would need to provide detailed answers to the questions posed. Alternatively, an institution might want a researcher developing a manuscript or poster about research with dual use potential to attest to having considered the risks and benefits of communicating that research; thus, it might be helpful to format the assessment framework with checkboxes to indicate that the points had been considered and perhaps to add a signature line. Scientific journals might find this "Points To

Consider” tool most useful as a hyperlink in whatever system the journal employs for instructing authors and manuscript reviewers, especially those reviewing for biosecurity concerns.

2. Principles for the Responsible Communication of Research With Dual Use Potential

1. The open and unfettered sharing of information and technologies has been a hallmark of the life sciences and has fostered a steady stream of scientific advances that underpin public health and safety, a strong and safe food supply, a healthy environment, and a vigorous economy.

2. Progress in the life sciences relies heavily on the communication of research findings so that the findings can be both validated and used for further research.

3. Life sciences research should be communicated to the fullest extent possible to ensure the continued advancement of human, animal, plant, and environmental health. Consequently, any restriction of scientific communication should be the rare exception rather than the rule.

4. There is a need for reasonable balance in decisions about the communication of research with dual use potential. It is important to recognize the potential for the deliberate and malevolent misuse of dual use research findings and to consider whether the disclosure of certain information might reasonably pose a threat to national security (i.e., public health and safety, agricultural crops and other plants, animals, the environment, or materiel). If the communication of dual use research *does* pose potential security risks, the logical next step is a risk-benefit analysis of communicating the information.

5. After weighing the risks and benefits of communicating dual use research findings, the decision regarding communication is not necessarily a binary (yes/no) one. Rather, a range of options for communication should be identified and considered. The options available will depend on the research setting (e.g., academia, government, or private). They could range from full and immediate communication, to delayed and/or modified communication, to restricted/no communication, and could be recommended singly or in appropriate combinations on a case-by-case basis, depending on the nature of the dual use finding and the potential risks associated with its communication.

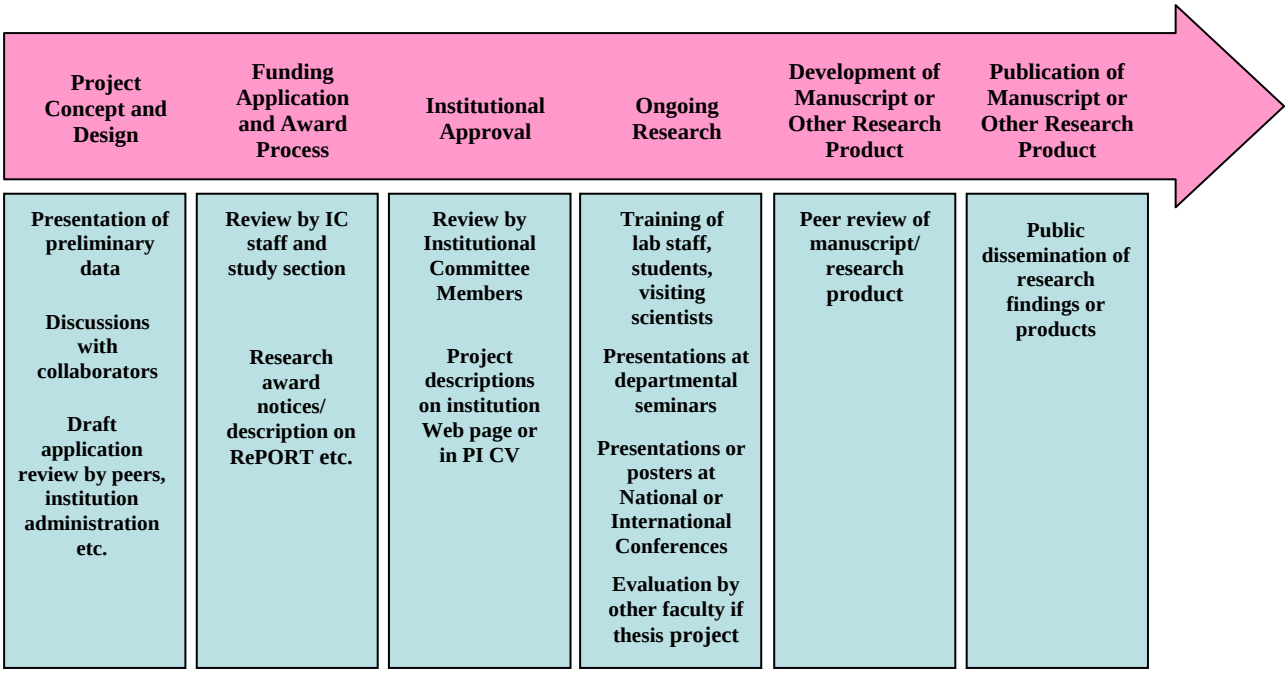
6. Paradigms for the responsible communication of research with dual use potential should also take into consideration that the communication of dual use research can occur at multiple points throughout the research process, that is, at points well upstream of the publication stage (see Figure 1 below). Thus, it is important to apply principles and practices of responsible communication at these early stages as well.

7. It is important to consider not only *what* is communicated but also the *way* in which it is communicated. Investigators and sponsors of research with dual use potential should recognize that the communication of certain dual use information is likely to raise biosecurity concerns, not only within the scientific community but also within the general public. Consideration should be given to the potential for public concern and misunderstanding and for sensationalism. Thought should be given to the need for the

inclusion of contextual and explanatory information that might minimize such concerns and misunderstanding.

8. Public trust is essential to the vitality of the life sciences research enterprise. It has always been important for life scientists to participate in activities that enhance public understanding of their research. However, because of the potential for public misunderstanding of and concerns about dual use research, it is especially important that life scientists conducting research with dual use potential engage in outreach on a regular basis to increase awareness of the importance of the research and to reassure the public that the research is being conducted and communicated responsibly.

Figure 1. Examples of Points of Communication of Dual Use Research During the Research Process



3. Points To Consider in Risk Assessment and Management of Research That is Potentially Dual Use of Concern

Could this research yield information that could be intentionally misused to threaten public health and safety or other aspects of national security?

- What is the nature of that information?
- Is the information novel?
- Is the information applicable to other, perhaps common, organisms, biologics, etc.?
- Could the information be directly misused to pose a threat? For example, even if the information would need to be combined with other information/technologies in order to pose a threat, is that other information/technology currently available?
- Does the information need to be combined with other information to pose a threat?
- If so, is that other information already available?

What is the nature of the threat that could be posed from intentional misapplication of the information, and what are the potential consequences?

- What is the potential nature (e.g., economic, agricultural, public health, and/or public terror), and what is the potential impact of the threat?
- What is the scope of the potential threat (i.e., how many/which people, plants, animals might be adversely affected)?
- Are there currently countermeasures for this threat?
- What type of technical expertise and/or physical resources would be needed to apply the information for malevolent purposes?
- In what timeframe might the information be misused? Is there concern about immediate or near-future potential use, or is the concern about misuse in the distant future?
- Would it require a low or high degree of technical skill and sophistication to use the dual use information for harmful purposes?

Based on the above considerations, how likely (reasonably anticipated) is it that the information could be used to pose a threat to public health and safety or other aspects of national security?

(If there is no discernable potential threat, then there is no need to continue the analysis.)

Could this research yield information that could potentially benefit the life sciences and/or public health and safety and other aspects of national security?

- If so, what is the nature of that information?
- What is the nature of the potential benefit?
- How much of a benefit might there be?

Do the potential risks outweigh the potential benefits?

- If not, determine applicable risk management strategies (see below).
- If so, consider whether the research should be modified or discontinued.

Potential Risk Management Strategies (more than one may be applicable)

- Ongoing review or monitoring of research
- Modification of experiment (e.g., can an alternative antibiotic or a different strain of organism be used?).
- Discontinuation of experiment. This may need to be discussed at a higher level, either within the local institution or at the federal level.
- Utilize the "Points to Consider in Assessing the Risks and Benefits of Communicating Research Information With Dual Use Potential" (Section 4):
  - Identify and assess the risks and benefits of communicating research with dual use potential
  - Weigh the risks versus the benefits
  - Formulate a decision for responsible communication; address the content, timing, and extent of communication
- Develop a comprehensive communication plan:
  - Consider the need to address the following issues in a communication:
    - The significance of the research findings for public health and safety, agriculture, the environment, and/or materiel
    - How the new information or technology will be useful to the scientific community
    - The biosafety measures in place as the research was conducted
    - The communication of less detailed findings
    - The dual use aspects of the information and that careful consideration was given to the biosecurity concerns in the decision to publish
  - Determine whether additional venues are appropriate for conveying the research information and contextual/background information.

4. Points To Consider in Assessing the Risks and Benefits of Communicating Research Information with Dual Use Potential

The NSABB developed this tool to guide researchers, manuscript reviewers, and others in identifying and assessing the risks and benefits of communicating research information that may be dual use of concern. This tool includes a series of questions that can be considered as well as options for the communication of research information judged to be dual use of concern

1. *General Overview of the Research Information With Dual Use Potential*
    a. What information is provided?
    b. To what extent is it novel?

2. *Risk Analysis*
    a. Are there reasonably anticipated risks to public health and safety from direct misapplication of this information?
        i. E.g., is novel scientific information provided that could be intentionally misused to threaten public health and/or safety?
        ii. E.g., does the information point out a vulnerability in public health and/or safety preparedness?
    b. Is it reasonably anticipated that this information could be directly misused to pose a threat to agriculture, plants, animals, the environment, or materiel (i.e., does the information point out a vulnerability with respect to agriculture, plants, animals, the environment, or materiel)?
    c. If a risk has been identified, in what timeframe (e.g., immediate, near future, years from now) might this information be used to pose a threat to public health and/or safety, agriculture, plants, animals, the environment, or materiel?
    d. If the information were to be broadly communicated "as is," what is the potential for:
        i. Public misunderstanding, that is, what might be the implications (e.g., psychological, social, health/dietary decisions, economic, commercial) of such misunderstandings?
        ii. Sensationalism (i.e., in what way might it result in widespread concern or even panic about public health or other safety/security issues?)

If no risk has been identified, no further dual use communication considerations are necessary. If a risk has been identified, continue on.

3. *Benefit Analysis*
    a. Are there potential benefits to public health and/or safety from application or utilization of this information?
    b. Are there potential benefits of the information for agriculture, plants, animals, the environment, or materiel (e.g., what potential solution does it offer to an identified problem or vulnerability)?
    c. Will this information be useful to the scientific community? If so, how?
    d. If a benefit has been identified, in what timeframe (e.g., immediate, near future, years from now) might this information be used to benefit science, public health, agriculture, plants, animals, the environment, or materiel?

4. *Risk versus Benefit Assessment*
   Based on the risks and benefits identified and considering the timeframe in which these might be realized:
   a. Do the benefits of communicating the information outweigh the risks?
   b. Do the risks outweigh the benefits?

5. *Formulation of Recommendation Regarding Communication*
   Decisions about how to responsibly communicate research with dual use potential should address content, timing, and possibly extent of distribution[1] of the information.
   a. Content
      i. Communicate as is.
      ii. Communicate with addition of appropriate contextual information. For example, it may be important to address:
         (1) The significance of the research findings for public health and/or safety, agriculture, the environment, or materiel
         (2) How the new information or technology will be useful to the scientific community
         (3) The biosafety measures in place as the research was conducted
         (4) The dual use potential of the information
         (5) The careful consideration that was given to the dual use concerns in the decision to publish
      iii. Recommend communicating a modified version of the product. For example, is it possible to "decouple" the material that poses security concerns from some or all of the potentially useful scientific information, or should specific information be removed (e.g., technical details about an enabling technology)?
   b. Timing
      i. Communicate immediately.
      ii. Recommend that communication be deferred until a clearly defined and agreed-upon endpoint is reached (e.g. a condition is met such that communication no longer poses the same degree of risk).

   c. Distribution[2]
      i. No limit on distribution.
      ii. Limit access to selected individuals on a "need to know" basis. It will be necessary to identify categories of individuals who should have access and under what circumstances.
      iii. Recommend that the product not be published or otherwise made accessible to the public.

[1]The relevance and/or feasibility of considering limits on the distribution of dual use research will depend on the specific situation (e.g., timing of the communication in terms of the maturity of the research, the nature of the information and the risks associated with its communication, and the relevant audience for the information). For example, while limiting distribution is not a consideration for most scientific journals, it might be a reasonable consideration early on in a research project that yielded information of special significance to public health or homeland security experts and for which countermeasures might need to be initiated prior to broader communication of the information.
[2]Ibid.

5. Considerations in the Development of a Communication Plan

Because of the potential for misuse of dual use research results, concerns on the part of the public, including members of the scientific community, about the sharing of such information can be anticipated. In addition, the public is increasingly sensitive to issues pertaining to research involving dangerous microbes and the risk of accidental or intentional release of such agents. A lack of public understanding and appreciation for the reason for conducting and communicating dual use research, sensationalism of dual use research findings, and concerns about public safety and national security all serve to undermine public trust in the life sciences research enterprise. Therefore, it is the responsibility of the scientific community to ensure that dual use research results and technologies are communicated responsibly.

Depending on the nature of the dual use research result/technology being communicated and the potential impact of communicating the information, it may be prudent to consider steps to maximize public understanding of, and appreciation for, the research effort and the decision to communicate the information. This can be achieved through the development of a plan for the responsible communication of dual use research information. For example, it may be important to address the following issues, both in the content of the work product and in the activities associated with dissemination of the work product:

- The significance of the research findings for public health and/or safety, agriculture, the environment, or materiel
- How the new information or technology will be useful to the scientific community
- The biosafety measures in place during the conduct of the research
- The dual use aspects of the information and the careful consideration given to biosecurity concerns in the decision to publish

In addition to including this type of information in the content of the work product, the following are some additional means for conveying the types of contextual information listed above. These means can be employed either singly or in any combination as deemed appropriate:

- Editorials are useful tools for providing contextual information, messages, and opinions. Editorials may be in the journal that publishes the dual use research manuscript. This type of editorial could be written by an individual who is not directly involved with the work, perhaps is not even in the same field, but who is nevertheless held in high regard by the scientific community. The editorial might speak to the significance of the research findings for public health, agriculture, the environment, or materiel; how the new information or technology will be useful to the scientific community; and the biosafety measures in place as the research was carried out and might acknowledge the dual use aspects of the information and that careful consideration was given to the biosecurity concerns in the decision to publish.

  Editorials may also be in the popular press and issued at the same time as the manuscript or shortly afterwards. This type of editorial would be geared toward the general public and should be written in nontechnical language to the greatest extent possible.

Nevertheless, it should address the same issues as described above (i.e., the nature and importance of the scientific discovery/technology; the significance of the research findings for public health, agriculture, the environment, or materiel; the safety precautions in place as the work was conducted; the dual use aspects of the information; and the consideration that was given to the biosecurity concerns in the decision to publish). Ideally, the author would be an individual who is known to and trusted by the general public.

- Press releases are commonly used by research institutions to highlight significant scientific advances for the media. They also provide an opportunity to provide contextual information (regarding issues that may be of concern to the public) and scientific perspectives on the findings (via quotes from other scientists). If the project involves investigators from multiple institutions, it will be important to coordinate the preparation and release of the announcement. In addition to including a description of the findings and their scientific significance, a press release might also address the significance of the research findings for public health, agriculture, the environment, or materiel; the biosafety and biocontainment measures in place as the work was conducted; the dual use aspects of the information; and the consideration that was given to the biosecurity concerns in the decision to publish.

- A press conference is usually reserved for highlighting the most significant and/or sensitive advances and provides an opportunity for direct interaction with the media. The investigator(s) and institutional representatives are usually present, but press conference organizers also should consider having other experts on hand who can address questions about the potential for misuse of the dual use information, biosafety, etc. A press release is usually provided to the media at a press conference (see above), but additional relevant materials can also be made available, such as backgrounders and fact sheets.

- Questions and Answers are useful tools for preparing to respond to queries from the press, the general public, or others. They might address:
    - The nature of the dual use advance
    - Reasons for conducting the work
    - Whether the public is/was at risk from the work
    - The potential for misuse of the research findings
    - Safety procedures utilized during experimentation
    - The review process prior to publication

- Talking Points are developed and employed for responding to questions from the press, the general public, or others. Talking points might include:
    - An explanation of the biosafety and biocontainment conditions that were employed to safeguard laboratory workers and the public (if applicable)
    - Acknowledgment that, along with significant benefits (to public health, agriculture, the environment, or materiel) of sharing the information widely, there are also some potential risks to publicly disseminating the information
    - Assurances that the national security implications of making such information publicly available was thoroughly considered

- A description of how the information contained within the research findings is critical for developing public health countermeasures

6. Criterion and Considerations for Identifying Dual Use Research of Concern

The biosecurity concerns that the NSABB is tasked with addressing pertain to the misapplication of information, technologies, or biological agents resulting from legitimate dual use research, not the conduct of the research itself. The goal of identifying dual use research of concern is to initiate a process aimed at reducing the potential that knowledge, products, or technology derived from certain life sciences research could be misapplied to threaten public health and safety or other aspects of national security. To facilitate consistent determinations of the dual use potential of research, the NSABB developed a criterion as a tool for those involved in any aspect of life sciences research.

During the process of developing the criterion, the NSABB identified a number of considerations and key concepts that are discussed below and are reflected in the final criterion:

- Because arguably most life sciences research has some potential for dual use, the NSABB strove to delineate a threshold that would identify that subset of life sciences research with the highest potential for yielding knowledge, products, or technology that could be misapplied to threaten public health or other aspects of national security. This subset of research is referred to herein as "dual use research of concern."

- It is important to emphasize that evaluation of the dual use potential of research should be based on a *current understanding* of the implications of the research results and whether it is reasonable to anticipate that such information could be misapplied to pose a threat. The results of research are of concern when they can be directly misapplied to pose a threat.

- In addition, the NSABB focused on the *scope* of a potential threat as a key consideration in evaluating research for dual use potential. Thus, the criterion captures threats with *broad* potential consequences to public health or other aspects of national security (e.g., that threaten populations rather than individuals).

- It cannot be overemphasized that characterization of research as dual use research of concern should not be viewed pejoratively. Such a characterization does not automatically mean that this type of research should not be conducted or communicated, rather that the conduct and communication of that research should be carefully considered from the outset and throughout the research process. The oversight process is about the responsible conduct and communication of research, not the restriction of research.

- The concern regarding dual use research is that the information, technologies, or products developed from it could be misused to threaten national security. The NSABB found that there are many different understandings of the term "national security," so it identified the relevant aspects and used the collective terms. Thus, the criterion refers to the potential for threats to public health and safety, agricultural crops and other plants, animals, the environment, and/or materiel. This would include threats to farming, livestock, aquaculture, terrestrial and marine wildlife, companion animals, domestic and wild plants and trees, ecological systems, and other natural resources, as well as manmade resources.

- An evaluation of research for its dual use potential will require scientific expertise and logical, sound judgment about the probability or foreseeability that others could misapply/misuse research results. It is important to acknowledge, however, that any such evaluation is subjective and will be influenced by the individual's knowledge, experience, and judgment.

- Life sciences research is an extraordinarily dynamic field that encompasses many diverse disciplines; therefore, it will be important to periodically review the criterion and modify it as necessary to ensure its relevance in the face of new advances and technologies.

With these concepts in mind, the NSABB proposes the following criterion for identifying dual use research of concern:

Criterion for Identifying Dual Use Research of Concern

Research that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health and safety, agriculture, plants, animals, the environment, or materiel.

Determining the applicability of this criterion is a subjective and sometimes challenging task. To assist those who need to make a determination as to whether research is potentially dual use of concern, the NSABB also delineated some categories of information, products, or technologies that might be especially likely to meet the threshold within the criterion for dual use research of concern, and thus deserve careful consideration with regard to the applicability of the criterion. It is important to emphasize that not all research that fits the categories below is necessarily dual use research of concern; rather, it is research for which the criterion needs to be especially carefully considered. Moreover, it is also the case that research that does *not* fall into the categories below might also meet the criterion for being dual use research of concern.

Finally, it is important to acknowledge that the starting point for the categories below was the seven "experiments of concern" from the NRC report, *Biotechnology Research in an Age of Terrorism*.[3] However, the NSABB categories have a different purpose and meaning from those of the NRC report. In the NRC report, the seven experiments of concern are classes of experiments that the NRC Committee believed illustrated the types of endeavors or discoveries that would require review and discussion by informed members of the scientific and medical community before they are undertaken or, if carried out, before they are published in full detail. The NSABB categories in Section 7, which in some cases are modifications of the NRC categories, are descriptors of information**,** products, or technologies that, if produced from life sciences research, might define that research as meeting the criterion for being dual use research of concern. Therefore, such research should be especially carefully assessed for meeting the criterion for dual use research of concern.

[3] Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, National Research Council, *Biotechnology Research in an Age of Terrorism* (Washington, D.C.: The National Academies Press, 2004).

7. Categories of Research Warranting Assessment for DURC Potential

The NSABB categories are knowledge, products, or technologies that could enable any of the following:

1. ***Enhance the harmful consequences[4] of a biological agent[5] or toxin.[6]*** The rationale for this category is that enhancing the pathogenic consequences of an agent or toxin could increase the likelihood of disease and compromise the ability to treat the disease(s) they cause if extant therapeutics are no longer effective. Of note, enhancing the pathogenic consequences of an agent includes rendering a nonpathogenic microbe pathogenic. Information that would fall into this category and would likely be considered dual use of concern would be how to make a seasonal strain of the influenza virus as deadly as the 1918 pandemic strain.

   An example of information that would fall under this category, but is unlikely to be dual use of concern, includes routine techniques for restoring the virulence of viral stocks by back-passaging in animal hosts, identification of virulence factors through genome-wide screening or gene knockout techniques, and standard genetic manipulation to study the virulence of an organism.

2. ***Disrupt immunity[7] or the effectiveness of an immunization[8] without clinical and/or agricultural justification.*** The rationale for this category is that immunity is a key component in a host's defense against pathogens and toxins, thus rendering an immunization ineffective or disrupting immunity could have harmful consequences for public health, agricultural crops and other plants, and animals. For instance, rendering an immunization ineffective could make a host population vulnerable to the pathogenic consequences of a microbe from which the host population would have otherwise been protected or for which protection, such as a vaccine, was available.

---

[4]*Harmful consequences:* The ability of a biological agent or toxin to critically alter normal biological functions, inflict damage on public health resources, materiel, and public safety. This would include augmenting properties such as virulence, infectivity, stability, transmissibility, or the ability of the biological agent or toxin to be disseminated.

[5]*Biological agent:* As is consistent with 18 U.S.C. § 178, "any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae or protozoa), or infectious substance, or any naturally occurring, bioengineered or synthesized component of any such microorganism or infectious substance, capable of causing - (A) death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; (B) deterioration of food, water, equipment, supplies, or material of any kind; or (C) deleterious alteration of the environment; . ."

[6]*Toxin:* As is consistent with 18 U.S.C. § 178, "the toxic material or product of plants, animals, microorganisms (including, but not limited to, bacteria, viruses, fungi, rickettsiae or protozoa), or infectious substances, or a recombinant or synthesized molecule, whatever the origin and method of production, and includes - (A) any poisonous substance or biological product that may be engineered as a result of biotechnology that is produced by a living organism; or (B) any poisonous isomer or biological product, homolog, or derivative of such a substance; . ."

[7]*Immunity:* Encompasses all aspects of host immunity (e.g., active, adaptive, adoptive, passive, innate, and immune modulators).

[8]*Immunization:* Refers to the active or passive induction of immunity through inoculation (e.g., natural inoculation or vaccination) with an immunizing agent or with antibodies; this includes antitoxins and toxoids.

An example of information that fits this category and might qualify as dual use of concern is the insertion of an immunosuppressive cytokine into a viral genome to render the antiviral immune response less effective. Information about the immunosuppressive properties of chemotherapeutic drugs for cancer or autoimmune disorders could also fit this category, although it is unlikely to be dual use of concern.

3. ***Confer to a biological agent or toxin, resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions[9] against that agent or toxin or facilitate their ability to evade detection methodologies.*** The main concept is that anything that might compromise the ability to detect, treat, or prevent disease or illness (human or agricultural) caused by biological agents or toxins could result in a significant public health and/or economic burden.

   Examples of information that might fit this category and be considered dual use of concern include conferring doxycycline resistance to *Vibrio vulnificus* or conferring antibiotic resistance to agriculturally relevant microbes, such as rendering *Ralstonia solanacearum* (a bacterium on the U.S. Department of Agriculture list of high-consequence organisms) resistant to rifampin. Examples of research that might fit this category, but are unlikely to be dual use of concern, include the use of standard laboratory selection procedures with antibiotics using host-vector systems that do not present a significant risk to health or the environment (e.g., transforming a nonpathogenic/nontoxigenic *Escherichia coli* strain with a construct for the expression of a nontoxin protein or conferring rifampin resistance to *Pseudomonas fluorescens*).

4. ***Increase the stability,[10] transmissibility,[11] or the ability to disseminate[12] a biological agent or toxin.*** The rationale for this category is that increasing an agent's stability, transmissibility, or ability to disseminate could facilitate the purposeful malevolent use of a biological agent or toxin and increase the rate or ease by which an agent could spread, impeding attempts to contain disease outbreak. Uncontained outbreaks could lead to a large infected host population, which may not receive adequate care and treatment due to limited resources, allowing the disease to spread. Effective dissemination of a pathogenic agent or toxin could result in large-scale exposure and the inability to prevent or treat ensuing disease and/or damage in a host population.

---

[9]*Clinically and/or agriculturally useful prophylactic or therapeutic interventions:* Includes first- or second-line prevention and treatment measures or alternative therapeutics used with special populations (e.g., pregnant women and pediatric patients) in the form of vaccines, antibiotics, antivirals, antiparasitics, antibodies, herbicides, fungicides, algaecides, insecticides, etc. "Agriculture" encompasses all methods of production and management of livestock, crops, vegetation, and soil. Therefore, useful prophylaxes and therapeutics would include herbicides, fungicides, algaecides, insecticides, rodenticides, etc.

[10]*Stability:* The ability of a biological agent to remain viable when exposed to various environmental factors, including temperature, relative humidity, atmospheric pollution, and sunlight. Stability also includes persistence in a host.

[11]*Transmissibility:* The ease with which an agent spreads from host to host or from vector to host, e.g., via arthropod vectors.

[12]*Dissemination:* The process by which infectious diseases or toxins are dispersed. The same routes of entry pertinent to the natural spread of diseases are also relevant when their etiologic agents are delivered intentionally (e.g., inhalation of biological agent disseminated as an aerosol or ingestion of a biological agent disseminated through a water supply).

The inability to prevent or treat the disease or toxicity due to the lack of resources or therapeutics could result in a significant threat to the health of the host population(s). Of note, this category includes transmission between hosts of the same species or between hosts of differing species. The use of the term "weaponization" was carefully considered for this category, but since the term is not uniformly understood within the life sciences community, the concept of dissemination, which is a key component of weaponization, seems more appropriate.

Examples of research that falls within this category and that might be considered dual use of concern include changing genetic factors to increase transmissibility and altering the route of transmission or vector to increase the ease and effectiveness by which an agent may be transmitted. With regard to increasing the capability of an agent or toxin to be disseminated, there are inherent challenges in deciding whether information that falls into this category is dual use of concern. Some of the challenge relates to issues of scale and intent. For example, work on vectors to increase their activity for gene therapy may also enable the wide-scale dissemination of a pathogenic agent or toxin. Research on adjuvants, methods, and tools for the increased efficacy of biocontrol agents in agriculture may also encompass work with equipment such as agricultural sprayers that may need to be examined for their dual use potential.

5. ***Alter the host range[13] or tropism[14] of a biological agent or toxin.*** The rationale for this category is that altering the host range or tropism of a pathogenic agent or toxin could endanger a host population that normally would not be susceptible. Prevention and therapy measures for the newly vulnerable host population may be lacking, possibly allowing for the uncontrolled spread of disease. An example of research information that would fall under this category and that may be dual use of concern includes converting nonzoonotic agents into zoonotic agents, altering the tropism of viruses, and expanding the varieties of the same plant that a pathogenic agent could infect. Certain vaccine research and the development of animal models for infectious disease, which may involve alterations of the host range or tropism, are unlikely to constitute dual use research of concern. Specifically, the attenuation of viruses for vaccine development, whereby the attenuation procedure relies on a change in host range to reduce human virulence, is unlikely to constitute dual use research of concern.

6. ***Enhance the susceptibility of a host population.[15]*** Information about rendering host populations more susceptible to the pathogenic consequences of an agent or toxin could be used to compromise immune responses and enable the acquisition and spread of disease on an epidemic scale. Of note, the distinction should be made that research applicable to this category would not alter the susceptibility of an individual host or research cohort but rather that of a host population.

[13]*Host range*: The number of different species or populations that can become infected by a biological agent, causing disease in the host or allowing the host to become a carrier.
[14]*Tropism*: The specificity of a biological agent or toxin for a particular host tissue or cell.
[15]*Host population*: A collection of organisms that constitutes a specific group or occurs in a specified habitat. In the context of the criteria, this phrase implies that the misapplication of the knowledge, products, or technologies derived from the research has the potential to broadly impact a population of host organisms.

Thus, examples of research information that would fall under this category and might be considered dual use of concern include creation of a stable recombinant *Lactobacillus casei* that could effectively block the host's ability to synthesize an important immune signal, such as tumor necrosis factor alpha, which may directly facilitate the evasion of normal host defenses. Examples of research that generates information unlikely to be considered dual use of concern are research on the systemic exposure to immunostimulatory and immunosuppressive DNA and their effect on host susceptibility to local inflammatory challenge, studies to develop immunosuppressive drugs for cancer or transplantation, and delivery of a small interfering ribonucleic acid (RNA) (siRNA)[16] to a mouse that makes it hypersensitive to ionizing radiation, an infectious agent, or a toxin.

7. ***Generate a novel pathogenic agent[17] or toxin or reconstitute an eradicated[18] or extinct[19] biological agent.*** The rationale for this category is that host populations may not be immune to novel agents and reconstituted eradicated agents and there may not be existing diagnostics or known or widely available prophylaxes or therapeutics for such agents.

   Examples that would fall into this category and that might be considered dual use of concern include the de novo construction of a microbial pathogen using wholly unique gene sequences or combinations of sequences that do not exist in nature and reconstitution of a pathogen that no longer exists in nature, such as the reconstruction of the 1918 pandemic influenza virus. Research that is not likely to be dual use of concern includes standard experimentation that generates knockouts, mutants, reassortants, complement strains, or infectious molecular clones of viruses that are similar to naturally occurring agents.

[16]*Small interfering RNA (siRNA):* Known as "short interfering RNA" or "silencing RNA"; a class of RNA molecules that play a variety of roles in biology, most notably, siRNA is involved in the RNA interference (RNAi) pathway where the siRNA interferes with the expression of a specific gene.
[17]*Novel agent:* An agent that has not existed previously and is considered unique based on biological or other properties and traits (e.g., genotype and phenotype). Novel agents of concern are those for which there is no known or widely available prophylactic or therapeutic interventions, those that could evade detection, or those for which there is no known immunity.
[18]*Eradicated agent:* A biological agent that has been exterminated through surveillance and containment resulting in the permanent reduction to zero of the worldwide incidence in the transmission of the agent and the infection/disease it causes; intervention measures are no longer needed. Eradicated agents are thought to no longer exist in circulation in plants, animals, or the environment. Note: Reconstituted eradicated agents of concern are those for which there are no known or widely available prophylactic or therapeutic interventions, those that could evade diagnostics, or those for which there is no known immunity.
[19]*Extinct agent:* These agents are thought to no longer exist in nature or in the laboratory.